

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>14/040-PCT</b>	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. <b>PCT/EP 97/ 06268</b>	International filing date (day/month/year) <b>11/11/1997</b>	Priority date (day/month/year) <b>14/11/1996</b>
International Patent Classification (IPC) or national classification and IPC <b>C12N15/12</b>		
Applicant <b>BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


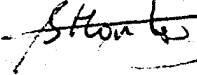
2. This **REPORT** consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand <b>23/05/1998</b>	Date of completion of this report <b>1 8. 02. 99</b>
Name and mailing address of the IPEA/  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Netherlands Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl Fax: (+31-70) 340-3016	Authorized officer  <b>B. Montero</b> Telephone No.

## I. Basis of the report

1. This report has been drawn up on the basis of *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.)*

☒ the international application as originally filed

☐

☐ the description, pages

as originally filed

pages

filed with the demand

pages

filed with the letter of

☐ the claims, Nos.

as originally filed

Nos.

as amended under Article 19

Nos.

filed with the demand

Nos.

filed with the letter of

☐ the drawings, sheets / fig.

as originally filed

sheets / fig.

filed with the demand

sheets / fig.

filed with the letter of

2. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.

☐ the drawings, sheets / fig.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2 (c)).

4. Additional observations, if necessary:

## IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees the applicant has:

- ☐ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

The present application relates to the human Anaphase Promoting complex. The article "Proceedings of the National Academy of Sciences USA" 1993, 90(21), pages 10031-10035 describes the identification of the human homolog of *Saccharomyces cerevisiae* CDC27, a subunit of the Anaphase Promoting Complex. Moreover, the article "Cell" 1995, 81(2), pages 261-268 discloses the human homologues of CDC27 and CDC16, a further subunit of the APC complex.

In view of the prior art a problem underlying the present invention can be defined as providing a further method for identifying subunits of the human APC complex. The solution proposed is as follows:

a) Method for identifying further subunits of the human APC complex making use of epitope-tagged genes. Claims 1-4.

A further problem relates to the method of producing recombinant APC and providing uses therefore. The solution proposed as formulated in the claims is as follows:

b) Method for producing recombinant APC and use thereof in a screening method. Claims 5-10.

Since methods for identifying the human homologues of *Saccharomyces cerevisiae* APC complex subunits are already known in the art, given the essential difference between the

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

problems posed and their corresponding solutions, and since no other technical features can be distinguished which, in the light of the prior art, could be regarded as special technical features, new and common to the identified problems and corresponding solutions, the IPEA considers that there is no single inventive concept underlying the plurality of claimed inventions of the present application (See Rule 13.1 PCT).

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☒ all parts.
- ☐ the parts relating to claims Nos.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement

## 1. Statement

Novelty	Claims	1-10	YES
	Claims		NO
Inventive Step	Claims	1-4	YES
	Claims	5-10	NO
Industrial Applicability	Claims	1-10	YES
	Claims		NO

## 2. Citations and Explanations

Reference is made to the following documents:

D1: Proceedings of the National Academy of Sciences USA, 1993, vol. 90, pages 10031-10035

D2: Molecular Biology of the Cell, 1996, vol. 7, pages 791-801

1. Claims 1-4 of the present application refer to a method for identifying novel subunits of the human Anaphase Promoting complex making use of epitope-tagged genes. No such method has been disclosed in the state of the art, and therefore claims 1-4 are novel and comply with the requirements of Article 33(2) PCT.

1.1. Document D1, which is considered to represent the most relevant state of the art, discloses a method for identifying human homologs of yeast genes by cross-referencing of yeast genes to mammalian chromosome maps. The method is applied to identify the human homolog of CDC27, a subunit of the *Saccharomyces cerevisiae* Anaphase promoting complex. In the light of the prior art the problem to be solved would be how to provide an alternative method for identifying subunits of the human APC complex. The solution disclosed by the applicant in claims 1-4 involves the use of epitope-tagged genes. No hint can be found in the state of the art which would prompt the skilled person to develop such a method. In consequence, claims 1-4 involve an inventive step and meet the requirements of Article 33(3) PCT.

2. Claims 5-10 relate to a method for producing recombinant APC and its use in a screening

method. Since the APC complex has not been obtained in the art using recombinant methods, it is considered that the subject-matter of claims 5-10 is novel and meets the requirements of Article 33(2) PCT.

2.1. Claims 5 and 6 refer to a method for producing recombinant APC by expressing cDNAs encoding APC subunits in a host. Document D1, which is considered to represent the most relevant state of the art, discloses (cf. page 10032, col. right, par. 2 - page 1033, col. left, par. 2) the identification of the human homolog of APC subunit CDC27. The problem to be solved by the present invention may therefore be regarded as how to provide a method for producing recombinant APC. The solution proposed in Claim 5, expression of cDNAs encoding APC subunits in a suitable host, cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons. Since the state of the art discloses in document D1 a method for identifying DNAs encoding human homologs of the yeast APC subunits, it would suffice to the skilled person to express them in a suitable host following standard methods in order to obtain a recombinant APC. A Baculovirus expression system as specified in claim 6 constitutes as well a routine expression system in the art. Claim 5 and 6, therefore, do not involve an inventive step and do not meet the requirements of Article 33(3) PCT.

2.2. Claims 7-10 refer to the use of a recombinant APC in a screening method for identifying substances which inhibit rapidly proliferating cells by interfering with the cell's entry into the subsequent cell cycle. Document D2, which is considered to represent the most relevant state of the art, discloses (cf. page 795, col. right, par. 2 - page 799, col. right, par. 3) a screening method in which yeasts extracts are employed to show ubiquitination of the cyclin Cib2, from which the subject-matter of claims 7-10 differs in that no recombinant APC is used. The problem to be solved by the present invention may therefore be regarded as how to provide an alternative screening test to the one disclosed in the state of the art. In the light of D1, which discloses a method for identifying human APC subunits, it would be obvious to the skilled person that a recombinant APC can be applied to the screening method of D1. It is therefore considered that claims 7-10 do not involve an inventive step and do not meet the requirements of Article 33(3) PCT.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No

PCT/EP97/06268

VII. *Certain defects in the international application*

The following defects in the form or contents of the international application have been noted:

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made.

1. Claim 7 refers to the use of recombinant APC in a screening method without specifying any features relating to how the method is to be performed which introduces a lack of clarity contrary to Article 6 PCT.



# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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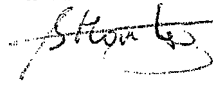
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Date of submission of the demand <b>23/05/1998</b>	Date of completion of this report <b>18.02.99</b>
Name and mailing address of the IPEA/  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Netherlands Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl Fax: (+31-70) 340-3016	Authorized officer  <b>B. Montero</b> Telephone No.

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pages

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- ☐ the claims, Nos.

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Nos.

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- ☐ the drawings, sheets / fig.

. as originally filed

sheets / fig.

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

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International application No.

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☐ the parts relating to claims Nos.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty	Claims	1-10	YES
	Claims		NO
Inventive Step	Claims	1-4	YES
	Claims	5-10	NO
Industrial Applicability	Claims	1-10	YES
	Claims		NO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP97/06268

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Claim 7 refers to the use of recombinant APC in a screening method without specifying any features relating to how the method is to be performed which introduces a lack of clarity contrary to Article 6 PCT.



## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 18 June 1998 (18.06.98)	
<b>International application No.</b> PCT/EP97/06268	<b>Applicant's or agent's file reference</b> 14/040-PCT
<b>International filing date</b> (day/month/year) 11 November 1997 (11.11.97)	<b>Priority date</b> (day/month/year) 14 November 1996 (14.11.96)
<b>Applicant</b> NASMYTH, Kim et al	

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

23 May 1998 (23.05.98)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<b>The International Bureau of WIPO</b> 34, chemin des Colombettes 1211 Geneva 20, Switzerland	<b>Authorized officer</b> S. De Michiel
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>14/040-PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 97/ 06268</b>	International filing date (day/month/year) <b>11/11/1997</b>	(Earliest) Priority Date (day/month/year) <b>14/11/1996</b>
Applicant <b>BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).
2. ☒ Unity of invention is lacking (see Box II).
3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - ☐ filed with the international application.
  - ☐ furnished by the applicant separately from the international application,
    - ☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - ☐ Transcribed by this Authority
4. With regard to the title, ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - ☒ the text is approved as submitted by the applicant.
  - ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
  - Figure No.            ☐ as suggested by the applicant. ☒ None of the figures.
  - ☐ because the applicant failed to suggest a figure.
  - ☐ because this figure better characterizes the invention.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 97/06268

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4

Method for identifying novel subunits of APC

2. Claims: 5-10

Method for producing recombinant APC and use thereof in a screening method.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12Q1/68 C07K14/47 C12Q1/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KING, RANDALL W. ET AL: "A 20S complex containing CDC27 and CDC16 catalyzes the mitosis-specific conjugation of ubiquitin to cyclin B"</p> <p>CELL (CAMBRIDGE, MASS.) (1995), 81(2), 279-88 CODEN: CELLB5;ISSN: 0092-8674, 1995, XP002030310</p> <p>cited in the application</p> <p>* Summary *</p> <p>see page 282, right-hand column, paragraph 2 - page 284, right-hand column, paragraph 1</p> <p>see page 285, left-hand column, paragraph 2 - page 286, left-hand column, paragraph 2</p> <p>---</p> <p>-/--</p>	1-4

☒ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

30 July 1998

Date of mailing of the international search report

05. 08. 1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Montero Lopez, B

## INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>STUART TUGENDREICH ET AL.: "CDC27Hs colocalizes with CDC16Hs to the centrosome and mitotic spindle and is essential for the metaphase to anaphase transition" CELL, vol. 81, no. 2, 21 April 1995, pages 261-268, XP002030311 NA US cited in the application * summary * see page 261, right-hand column, paragraph 3 - page 262, left-hand column, paragraph 1 see page 265, right-hand column, paragraph 4 - page 266, right-hand column, paragraph 1</p>	1-4
A	<p>--- STEFAN IRNIGER ET AL.: "Genes involved in sister chromatid separation are needed for B-type cyclin proteolysis in budding yeast" CELL, vol. 81, no. 2, 21 April 1995, pages 269-277, XP002030312 NA US cited in the application see page 269, right-hand column, paragraph 5 - page 275, left-hand column, paragraph 1</p>	1-4
A	<p>--- J.R. LAMB ET AL.: "Cdc16p, Cdc23p and Cdc27p form a complex essential for mitosis" EMBO JOURNAL, vol. 13, no. 18, 15 September 1994, pages 4321-4328, XP002030313 EYNHAM, OXFORD GB cited in the application see the whole document</p>	1-4
A	<p>--- STUART TUGENDREICH ET AL.: "Linking yesat genetics to mammalian genomes: Identification and mapping of the human homolog of CDC27 via the expressed sequence tag (EST) data base" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 90, no. 21, 1 November 1993, pages 10031-10035, XP002030314 WASHINGTON US cited in the application see abstract see page 10032, right-hand column, paragraph 2 - page 10035, right-hand column, paragraph 1</p> <p>--- -/--</p>	1-4

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WOLFGANG ZACHARIAE ET AL.: "TPR proteins required for anaphase progression mediate ubiquitination of mitotic B-type cyclins in yeast"</p> <p>MOLECULAR BIOLOGY OF THE CELL, vol. 7, no. 5, May 1996, pages 791-801, XP000671428</p> <p>cited in the application</p> <p>see page 793, left-hand column, paragraph 3 - right-hand column, paragraph 1</p> <p>see page 794, left-hand column, last paragraph - page 795, right-hand column, paragraph 1</p>	5-10
P,X	<p>-----</p> <p>ZACHARIAE, WOLFGANG ET AL:</p> <p>"Identification of subunits of the anaphase - promoting complex of Saccharomyces cerevisiae"</p> <p>SCIENCE (WASHINGTON, D. C.) (1996), 274(5290), 1201-1204 CODEN: SCIEAS;ISSN: 0036-8075, 1996, XP002064238</p> <p>see abstract</p> <p>see page 1203, middle column, paragraph 1 - right-hand column, paragraph 1</p> <p>-----</p>	1-4

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>14/040-PCT</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 97/06268</b>	International filing date (day/month/year) <b>11/11/1997</b>	(Earliest) Priority Date (day/month/year) <b>14/11/1996</b>
Applicant  <b>BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☒ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the **title**, ☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

Figure No.            ☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.



# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 97/06268

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-4

Method for identifying novel subunits of APC

2. Claims: 5-10

Method for producing recombinant APC and use thereof in a screening method.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12Q1/68 C07K14/47 C12Q1/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KING, RANDALL W. ET AL: "A 20S complex containing CDC27 and CDC16 catalyzes the mitosis-specific conjugation of ubiquitin to cyclin B" CELL (CAMBRIDGE, MASS.) (1995), 81(2), 279-88 CODEN: CELLB5;ISSN: 0092-8674, 1995, XP002030310 cited in the application * Summary * see page 282, right-hand column, paragraph 2 - page 284, right-hand column, paragraph 1 see page 285, left-hand column, paragraph 2 - page 286, left-hand column, paragraph 2</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-4



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

30 July 1998

Date of mailing of the international search report

05. 08. 1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Montero Lopez, B

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>STUART TUGENDREICH ET AL.: "CDC27Hs colocalizes with CDC16Hs to the centrosome and mitotic spindle and is essential for the metaphase to anaphase transition" CELL, vol. 81, no. 2, 21 April 1995, pages 261-268, XP002030311 NA US cited in the application * summary * see page 261, right-hand column, paragraph 3 - page 262, left-hand column, paragraph 1 see page 265, right-hand column, paragraph 4 - page 266, right-hand column, paragraph 1</p>	1-4
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A	<p>STUART TUGENDREICH ET AL.: "Linking yesat genetics to mammalian genomes: Identification and mapping of the human homolog of CDC27 via the expressed sequence tag (EST) data base" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 90, no. 21, 1 November 1993, pages 10031-10035, XP002030314 WASHINGTON US cited in the application see abstract see page 10032, right-hand column, paragraph 2 - page 10035, right-hand column, paragraph 1</p>	1-4

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

## A. CLASSIFICATION OF SUBJECT MATTER

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Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12Q C07K

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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search

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Date of mailing of the international search report

05. 08. 1998

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Montero Lopez, B

## INTERNATIONAL SEARCH REPORT

International Application No

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-/--

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06268

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## PATENT COOPERATION TREATY

EINGELANGT

15. Juni 1998

PCT Patentstelle

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BOEHRINGER INGELHEIM GMBH  
A Patente  
Postfach 200  
D-55216 Ingelheim/Rhein  
ALLEMAGNENOTIFICATION OF RECEIPT  
OF DEMAND(PCT Rule 61.1(b), first sentence  
and Administrative Instructions, Section 601)

Eingang A-Patente

08. Juni 1998

SB gesehen erledigt Date of mailing  
(day/month/year)

05.06.98

Applicant's or agent's file reference

14/040-PCT

## IMPORTANT NOTIFICATION

International application No.

PCT/EP 97/06268

International filing date (day/month/year)

11/11/1997

Priority date (day/month/year)

14/11/1996

Applicant

BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

23/05/1998

2. This date of receipt is:



the actual date of receipt of the demand.



the date on which the proper corrections to the demand were timely received.

3. ☐ This date is AFTER the expiration of 19 months from the priority date.

**Attention:** The election(s) made in the demand does (do) not have the effect of postponing the commencement of the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22).

For details, see Annex B to Form PCT/IB/301 sent by the International Bureau and Volume II of the PCT Applicant's Guide.



This notification confirms the information given in person or by telephone on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/

European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Netherlands  
Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl  
Fax: (+31-70) 340-3016

Authorized officer

G.L.M. Kruydenberg  
070 - 3402277

Telephone No.

## PATENT COOPERATION TREATY

EINGELANGT

26. Feb. 1999

PCT Patentstelle

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BOEHRINGER INGELHEIM GMBH  
A Patente  
Postfach 200  
D-55216 Ingelheim/Rhein  
ALLEMAGNE

Eingang A Patente

24. Feb. 1999

NOTIFICATION OF TRANSMITTAL OF  
INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

18.02.99

Applicant's or agent's file reference

14/040-PCT

## IMPORTANT NOTIFICATION

International application No.

PCT/EP 97/06268

International filing date (day/month/year)

11/11/1997

Priority date (day/month/year)

14/11/1996

Applicant

BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Netherlands  
Tel.: (+31-70) 340-2040, Tx. 31 651 epo nl  
Fax: (+31-70) 340-3016

Authorized officer

Telephone No.

G.L.M. Kruidenberg  
070 - 3402277

Der Antrag ist bei der zuständigen mit der internationalen vorläufigen Prüfung beauftragten Behörde oder, wenn zwei oder mehr Behörden zuständig sind, bei der vom Anmelder gewählten Behörde einzureichen. Der Anmelder kann den Namen oder den Zweibuchstaben-Code der Behörde auf der nachstehenden Zeile angeben.

IPEA/

**PCT**

**KAPITEL II**

# **ANTRAG AUF INTERNATIONALE VORLÄUFIGE PRÜFUNG**

nach Artikel 31 des Vertrags über die internationale Zusammenarbeit auf dem Gebiet des Patentwesens:  
Der (die) Unterzeichnete(n) beantragt (beantragen), daß für die nachstehend bezeichnete internationale Anmeldung die internationale vorläufige Prüfung nach dem Vertrag über die internationale Zusammenarbeit auf dem Gebiet des Patentwesens durchgeführt wird.

Von der mit der internationalen vorläufigen Prüfung beauftragten Behörde auszufüllen

Bezeichnung der IPEA	Eingangsdatum des ANTRAGS
----------------------	---------------------------

<b>Feld Nr. I KENNZEICHNUNG DER INTERNATIONALEN ANMELDUNG</b>		Aktenzeichen des Anmelders oder Anwalts 14/040-PCT
Internationales Aktenzeichen PCT/EP 97/06268	Internationales Anmeldedatum (Tag/Monat/Jahr) 11. November 1997 (11.11.1997)	(Frühester) Prioritätstag (Tag/Monat/Jahr) 14. November 1996 (14.11.1996)
Bezeichnung der Erfindung METHODS FOR PRODUCING THE ANAPHASE PROMOTING COMPLEX		
<b>Feld Nr. II ANMELDER</b>		
Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)  BOEHRINGER INGELHEIM INTERNATIONAL GMBH Postfach 200 D-55216 Ingelheim am Rhein DE		Telefonnr.: 06132/772282  Telefaxnr.: 06132/774377  Fernschreibnr.: 4187910 bi d
Staatsangehörigkeit (Staat): DE		Sitz oder Wohnsitz (Staat): DE
Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)  NASMYTH, Kim Sonnenfelsgasse 5/13 A-1010 Wien AT		
Staatsangehörigkeit (Staat): GB		Sitz oder Wohnsitz (Staat): AT
Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)  ZACHARIAE, Wolfgang Eduard Poetzl-Gasse 3-7/26 A-1190 Wien AT		
Staatsangehörigkeit (Staat): DE		Sitz oder Wohnsitz (Staat): AT
<input checked="" type="checkbox"/> Weitere Anmelder sind auf einem Fortsetzungsblatt angegeben.		

Fortsetzung von Feld Nr. II ANMELDER

*Wird keines der folgenden Felder benutzt, so ist dieses Blatt dem Antrag nicht beizufügen.*

Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)

GALOVA, Marta  
Kolschitzkygasse 14-18/4/3  
A-1040 Wien  
AT

Staatsangehörigkeit (Staat):

SK

Sitz oder Wohnsitz (Staat):

AT

Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)

Staatsangehörigkeit (Staat):

Sitz oder Wohnsitz (Staat):

Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)

Staatsangehörigkeit (Staat):

Sitz oder Wohnsitz (Staat):

Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)

Staatsangehörigkeit (Staat):

Sitz oder Wohnsitz (Staat):

☐ Weitere Anmelder sind auf einem zusätzlichen Fortsetzungsblatt angegeben.

**Feld Nr. III ANWALT ODER GEMEINSAMER VERTRETER; ZUSTELLANSCHRIFT**

- Die folgende Person ist ☐ Anwalt ☒ gemeinsamer Vertreter
- und ☒ ist vom (von den) Anmelder(n) bereits früher bestellt worden und vertritt ihn (sie) auch für die internationale vorläufige Prüfung.
- ☐ wird hiermit bestellt; eine etwaige frühere Bestellung eines Anwalts/gemeinsamen Vertreters wird hiermit widerrufen.
- ☐ wird hiermit zusätzlich zu dem bereits früher bestellten Anwalt/gemeinsamen Vertreter, nur für das Verfahren vor der mit der internationalen vorläufigen Prüfung beauftragten Behörde bestellt.

Name und Anschrift: (Familienname, Vorname; bei juristischen Personen vollständige amtliche Bezeichnung. Bei der Anschrift sind die Postleitzahl und der Name des Staats anzugeben.)

BOEHRINGER INGELHEIM INTERNATIONAL GMBH  
Postfach 200  
D-55216 Ingelheim am Rhein  
DE

Telefonnr.:

06132/772282

Telefaxnr.:

06132/774377

Fernschreibnr.:

4187910 b j d

- ☐ Dieses Kästchen ist anzukreuzen, wenn kein Anwalt oder gemeinsamer Vertreter bestellt ist und statt dessen im obigen Feld eine spezielle Zustellanschrift angegeben wird.

**Feld Nr. IV ERKLÄRUNG BETREFFEND ÄNDERUNGEN**

Der Anmelder wünscht, daß die mit der internationalen vorläufigen Prüfung beauftragte Behörde\*

- i) ☒ die internationale vorläufige Prüfung auf der Grundlage der internationalen Anmeldung in der ursprünglich eingereichten Fassung aufnimmt.
- ii) ☐ die Änderungen nach Artikel 34
- ☐ der Beschreibung (Änderungen liegen bei)
- ☐ der Ansprüche (Änderungen liegen bei)
- ☐ der Zeichnungen (Änderungen liegen bei)
- berücksichtigt.
- iii) ☐ die beim Internationalen Büro eingereichten Änderungen der Ansprüche nach Artikel 19 berücksichtigt (Kopie liegt bei).
- iv) ☐ die Änderungen der Ansprüche nach Artikel 19 nicht berücksichtigt, sondern als überholt ansieht.
- v) ☐ den Beginn der internationalen vorläufigen Prüfung bis zum Ablauf von 20 Monaten ab dem Prioritätsdatum aufschiebt, sofern die Behörde nicht eine Kopie nach Artikel 19 vorgenommener Änderungen oder eine Erklärung des Anmelders erhält, daß er keine solchen Änderungen vornehmen will (Regel 69.1 d)). (Dieses Kästchen darf nur angekreuzt werden, wenn die Frist nach Artikel 19 noch nicht abgelaufen ist.)

\* Wenn kein Kästchen angekreuzt wird, wird mit der internationalen vorläufigen Prüfung auf der Grundlage der internationalen Anmeldung in der ursprünglich eingereichten Fassung begonnen; wenn eine Kopie der Änderungen der Ansprüche nach Artikel 19 und/oder Änderungen der internationalen Anmeldung nach Artikel 34 bei der mit der internationalen vorläufigen Prüfung beauftragten Behörde eingeht, bevor diese mit der Erstellung eines schriftlichen Bescheids oder des internationalen vorläufigen Prüfungsberichts begonnen hat, wird jedoch die geänderte Fassung verwendet.

**Feld Nr. V BENENNUNG VON STAATEN ALS AUSGEWÄHLTE STAATEN**

- ☒ Der Anmelder benennt als ausgewählte Staaten alle auswählbaren Staaten (das heißt, alle Staaten, die bestimmt wurden und durch Kapitel II des PCT gebunden sind) ausgenommen .....
- .....
- .....
- (Möchte der Anmelder bestimmte Staaten nicht auswählen, sind die Namen oder Zweibuchstaben-Codes dieser Staaten auf den obenstehenden Zeilen anzugeben.)

**Feld Nr. VI KONTROLLISTE**

Dem Antrag liegen folgende Unterlagen für die Zwecke der internationalen vorläufigen Prüfung bei:

- |   |   |         |
|---|---|---------|
| 1. Änderungen nach Artikel 34                         |   |         |
| Beschreibung  | : | Blätter |
| Ansprüche   | : | Blätter |
| Zeichnungen   | : | Blätter |
| 2. Begleitschreiben zu den Änderungen nach Artikel 34 | : | Blätter |
| 3. Kopie der Änderungen nach Artikel 19               | : | Blätter |
| 4. Kopie einer Erklärung nach Artikel 19              | : | Blätter |
| 5. Sonstige (einzeln auführen) :                      | : | Blätter |

Von der mit der internationalen vorläufigen Prüfung beauftragten Behörde auszufüllen

erhalten                      nicht erhalten

<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>


Dem Antrag liegen außerdem die nachstehend angekreuzten Unterlagen bei:


- |  |   |
|--|---|
| 1. <input type="checkbox"/> unterzeichnete gesonderte Vollmacht        | 4. <input checked="" type="checkbox"/> Blatt für die Gebührenberechnung |
| 2. <input type="checkbox"/> Kopie der allgemeinen Vollmacht            | 5. <input type="checkbox"/> sonstige (einzeln auführen):                |
| 3. <input type="checkbox"/> Begründung für das Fehlen der Unterschrift |   |

**Feld Nr. VII UNTERSCHRIFT DES ANMELDERS, ANWALTS ODER GEMEINSAMEN VERTRETERS**

Der Name jeder unterzeichnenden Person ist neben der Unterschrift zu wiederholen, und es ist anzugeben, sofern sich dies nicht aus dem Antrag ergibt, in welcher Eigenschaft die Person unterzeichnet.

BOEHRINGER INGELHEIM INTERNATIONAL GMBH  
ppa.    i.A.

  
Dr. H.-G. Kläs

  
DI Christine Farniok

Von der mit der internationalen vorläufigen Prüfung beauftragten Behörde auszufüllen

- |  |   |
|--|---|
| 1. Datum des tatsächlichen Eingangs des ANTRAGS:   |   |
| 2. Geändertes Eingangsdatum des Antrags aufgrund von BERICHTIGUNGEN nach Regel 60.1.b):  |   |
| 3. <input type="checkbox"/> Eingangsdatum des Antrags NACH Ablauf von 19 Monaten ab Prioritätsdatum; Punkt 4 und Punkt 5, unten, finden keine Anwendung.                   | <input type="checkbox"/> Der Anmelder wurde entsprechend unterrichtet |
| 4. <input type="checkbox"/> Eingangsdatum des Antrags INNERHALB 19 Monate ab Prioritätsdatum wegen Fristverlängerung nach Regel 80.5.                                      |   |
| 5. <input type="checkbox"/> Das Eingangsdatum des Antrags liegt nach Ablauf von 19 Monaten ab Prioritätsdatum, der verspätete Eingang ist aber nach Regel 82 ENTSCHULDIGT. |   |

Vom Internationalen Büro auszufüllen

Antrag vom IPEA erhalten am:

## PCT

## BLATT FÜR DIE GEBÜHRENBERECHNUNG

## Anhang zum Antrag auf internationale vorläufige Prüfung

Von der mit der internationalen vorläufigen Prüfung  
beauftragten Behörde auszufüllenInternationales  
Aktenzeichen PCT/EP 97/06268Aktenzeichen des  
Anmelders oder Anwalts 14/040-PCT

Eingangsstempel der IPEA

Anmelder BOEHRINGER INGELHEIM INTERNATIONAL GMBH  
D-55216 Ingelheim an Rhein

## Berechnung der vorgeschriebenen Gebühren

1. Gebühr für die vorläufige Prüfung ..... 3.000,-- P

2. Bearbeitungsgebühr (Anmelder aus einigen Staaten  
haben Anspruch auf eine Ermäßigung der  
Bearbeitungsgebühr um 75%. Hat der Anmelder (oder  
haben alle Anmelder) einen solchen Anspruch, so  
beträgt der in Feld H einzutragende Betrag 25 % der  
Bearbeitungsgebühr.) ..... 285,-- H3. Gesamtbetrag der vorgeschriebenen Gebühren  
Addieren Sie die Beträge in den Feldern  
P und H und tragen Sie die Summe in  
das nebenstehende Feld ein ..... 3.285,-- DEM  
INSGESAMT

## Zahlungsart

☒ Abbuchungsauftrag für das  
laufende Konto bei der IPEA  
(siehe unten)☐ Barzahlung☐ Scheck☐ Gebührenmarken☐ Postanweisung☐ Kupons☐ Bankwechsel☐ Sonstige (einzeln angeben):

## Abbuchungsauftrag (diese Zahlungsweise gibt es nicht bei allen Behörden)

Die IPEA/ EP ☒ wird beauftragt, den vorstehend angegebenen Gesamtbetrag der Gebühren von meinem laufenden  
Konto abzubuchen.☒ (dieses Kästchen darf nur angekreuzt werden, wenn die Vorschriften der IPEA über laufende Konten dieses Verfahren  
erlauben) wird beauftragt, Fehlbeträge oder Überzahlungen des vorstehend angegebenen Gesamtbetrags  
der Gebühren meinem laufenden Konto zu belasten bzw. gutzuschreiben.

2800.0140

22.05.98

Boehringer Ingelheim GmbH  
ppa. i.A.

Kontonummer

Datum (Tag/Monat/Jahr)

Unterschrift

Eingang Patente		
25. Juni 1998		
SB	gesehen	erledigt
LR		PCT

## PATENT COOPERATION TREATY

INFORMATION CONCERNING ELECTED  
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

EINGELANGT

To:

29. Juni 1998

Patentstelle

BOEHRINGER INGELHEIM INTERNATIONAL  
GMBH  
Postfach 200  
D-55216 Ingelheim am Rhein  
ALLEMAGNE

Date of mailing (day/month/year) 18 June 1998 (18.06.98)		
Applicant's or agent's file reference 14/040-PCT		IMPORTANT INFORMATION
International application No. PCT/EP97/06268	International filing date (day/month/year) 11 November 1997 (11.11.97)	Priority date (day/month/year) 14 November 1996 (14.11.96)
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al		

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

EP : AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
National : CA, JP, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

National : MX

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent.

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. (41-22) 740.14.35</p>	<p>Authorized officer: S. De Michiel</p> <p>Telephone No. (41-22) 388.83.38</p>
---	---



Eingang A-Patente

# PATENT COOPERATION TREATY

02. Juni 1998

Sb	gesendet	empfangen
Ja		

PCT

From the INTERNATIONAL BUREAU

To:

08. Juni 1998

Patentstelle

BOEHRINGER INGELHEIM INTERNATIONAL  
GMBH  
Postfach 200  
D-55216 Ingelheim am Rhein  
ALLEMAGNE

## NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

Date of mailing (day/month/year) 22 May 1998 (22.05.98)		
Applicant's or agent's file reference 14/040-PCT		IMPORTANT NOTICE
International application No. PCT/EP97/06268	International filing date (day/month/year) 11 November 1997 (11.11.97)	Priority date (day/month/year) 14 November 1996 (14.11.96)
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

CA,EP,JP,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

MX

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 22 May 1998 (22.05.98) under No. WO 98/21326

### REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

### REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

EINGELANGT  
26.11.1998  
Patentstelle  
REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only	
International Application No.	PCT/EP 97 / 0 6 2 6 8
International Filing Date	11 NOV 1997, 11.11.97
EUROPEAN PATENT OFFICE PCT INTERNATIONAL APPLICATION	
Name of receiving Office and "PCT International Application"	
Applicant's or agent's file reference (if desired) (12 characters maximum) 14/040-PCT	

<b>Box No. I TITLE OF INVENTION</b>	
METHODS FOR PRODUCING THE ANAPHASE PROMOTING COMPLEX	
<b>Box No. II APPLICANT</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)	<input type="checkbox"/> This person is also inventor.
BOEHRINGER INGELHEIM INTERNATIONAL GMBH Postfach 200 D-55216 Ingelheim am Rhein DE	Telephone No. 06132/772282
	Facsimile No. 06132/774377
	Teleprinter No. 4187910 bi d
State (i.e. country) of nationality: DE	State (i.e. country) of residence: DE
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<b>Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)</b>	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)	This person is:
NASMYTH, Kim Sonnenfelsgasse 5/13 A-1010 Wien AT	<input type="checkbox"/> applicant only
	<input checked="" type="checkbox"/> applicant and inventor
	<input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)
State (i.e. country) of nationality: GB	State (i.e. country) of residence: AT
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box	
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.	
<b>Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>	
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input type="checkbox"/> agent <input checked="" type="checkbox"/> common representative	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	Telephone No.
Boehringer Ingelheim GmbH Postfach 200 D-55216 Ingelheim am Rhein DE	06132/772282
	Facsimile No.
	06132/774377
	Teleprinter No.
	4187910 bi d
<input type="checkbox"/> Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.	

## Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

*If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

ZACHARIAE, Wolfgang  
Eduard Poetzi-Gasse 3-7/26  
A-1190 Wien  
AT

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

DE

State (i.e. country) of residence:

AT

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

GALOVA, Marta  
Kolschitzkygasse 14-18/4/3  
A-1040 Wien  
AT

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

SK

State (i.e. country) of residence:

AT

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☒ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

☐ all designated States☐ all designated States except the United States of America☐ the United States of America only☐ the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☐ AP **ARIPO Patent:** GH Ghana, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☐ EA **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☐ OA **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- |   |   |
|---|---|
| <input type="checkbox"/> AL Albania                               | <input type="checkbox"/> LV Latvia                                    |
| <input type="checkbox"/> AM Armenia                               | <input type="checkbox"/> MD Republic of Moldova                       |
| <input type="checkbox"/> AT Austria                               | <input type="checkbox"/> MG Madagascar                                |
| <input type="checkbox"/> AU Australia                             | <input type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input type="checkbox"/> AZ Azerbaijan                            |   |
| <input type="checkbox"/> BA Bosnia and Herzegovina                | <input type="checkbox"/> MN Mongolia                                  |
| <input type="checkbox"/> BB Barbados                              | <input type="checkbox"/> MW Malawi                                    |
| <input type="checkbox"/> BG Bulgaria                              | <input checked="" type="checkbox"/> MX Mexico                         |
| <input type="checkbox"/> BR Brazil                                | <input type="checkbox"/> NO Norway                                    |
| <input type="checkbox"/> BY Belarus                               | <input type="checkbox"/> NZ New Zealand                               |
| <input checked="" type="checkbox"/> CA Canada                     | <input type="checkbox"/> PL Poland                                    |
| <input type="checkbox"/> CH and LI Switzerland and Liechtenstein  | <input type="checkbox"/> PT Portugal                                  |
| <input type="checkbox"/> CN China                                 | <input type="checkbox"/> RO Romania                                   |
| <input type="checkbox"/> CU Cuba                                  | <input type="checkbox"/> RU Russian Federation                        |
| <input type="checkbox"/> CZ Czech Republic                        | <input type="checkbox"/> SD Sudan                                     |
| <input type="checkbox"/> DE Germany                               | <input type="checkbox"/> SE Sweden                                    |
| <input type="checkbox"/> DK Denmark                               | <input type="checkbox"/> SG Singapore                                 |
| <input type="checkbox"/> EE Estonia                               | <input type="checkbox"/> SI Slovenia                                  |
| <input type="checkbox"/> ES Spain                                 | <input type="checkbox"/> SK Slovakia                                  |
| <input type="checkbox"/> FI Finland                               | <input type="checkbox"/> SL Sierra Leone                              |
| <input type="checkbox"/> GB United Kingdom                        | <input type="checkbox"/> TJ Tajikistan                                |
| <input type="checkbox"/> GE Georgia                               | <input type="checkbox"/> TM Turkmenistan                              |
| <input type="checkbox"/> GH Ghana                                 | <input type="checkbox"/> TR Turkey                                    |
| <input type="checkbox"/> HU Hungary                               | <input type="checkbox"/> TT Trinidad and Tobago                       |
| <input type="checkbox"/> IL Israel                                | <input type="checkbox"/> UA Ukraine                                   |
| <input type="checkbox"/> IS Iceland                               | <input type="checkbox"/> UG Uganda                                    |
| <input checked="" type="checkbox"/> JP Japan                      | <input checked="" type="checkbox"/> US United States of America       |
| <input type="checkbox"/> KE Kenya                                 |   |
| <input type="checkbox"/> KG Kyrgyzstan                            | <input type="checkbox"/> UZ Uzbekistan                                |
| <input type="checkbox"/> KP Democratic People's Republic of Korea | <input type="checkbox"/> VN Viet Nam                                  |
|   | <input type="checkbox"/> YU Yugoslavia                                |
| <input type="checkbox"/> KR Republic of Korea                     | <input type="checkbox"/> ZW Zimbabwe                                  |
| <input type="checkbox"/> KZ Kazakstan                             |   |
| <input type="checkbox"/> LC Saint Lucia                           |   |
| <input type="checkbox"/> LK Sri Lanka                             |   |
| <input type="checkbox"/> LR Liberia                               |   |
| <input type="checkbox"/> LS Lesotho                               |   |
| <input type="checkbox"/> LT Lithuania                             |   |
| <input type="checkbox"/> LU Luxembourg                            |   |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- ☐ .....
- ☐ .....
- ☐ .....
- ☐ .....
- ☐ .....

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of .....

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

**Supplemental Box**      *If the Supplemental Box is not used, this sheet need not be included in the request.*

*Use this box in the following cases:*

**1. If, in any of the Boxes, the space is insufficient to furnish all the information:**

*in particular:*

- (i) *if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available:*
- (ii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked:*
- (iii) *if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:*
- (iv) *if, in addition to the agent(s) indicated in Box No. IV, there are further agents:*
- (v) *if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part":*
- (vi) *if there are more than three earlier applications whose priority is claimed:*

*in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;*

*in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below;*

*in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*

*in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*

*in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;*

*in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*

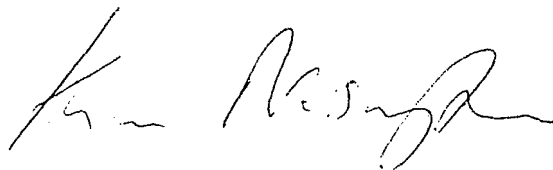
*in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.*

**2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:**

*in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.*

Continuation of Box No. IX

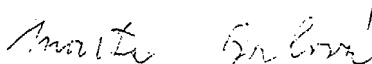
NASMYTH, Kim



ZACHARIAE, Wolfgang



GALOVA Marta



**Box No. VI PRIORITY CLAIM**Further priority claims are indicated in the Supplemental Box ☐

The priority of the following earlier application(s) is hereby claimed:

Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) DE	(14.11.1996) 14. Nov. 1996	96118297.9	European Patent Office
item (2)			
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

☐ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s):
**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA /

Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office):

Date (day/month/year):

Number:

**Box No. VIII CHECK LIST**

This international application contains the following number of sheets:

1. request : 5 sheets  
 2. description : 39 sheets  
 3. claims : 2 sheets  
 4. abstract : 1 sheets  
 5. drawings : 22 sheets  
 Total : 69 sheets

This international application is accompanied by the item(s) marked below:

1. ☐ separate signed power of attorney  
 2. ☐ copy of general power of attorney  
 3. ☐ statement explaining lack of signature  
 4. ☐ priority document(s) identified in Box No. VI as item(s):  
 5. ☒ fee calculation sheet  
 6. ☐ separate indications concerning deposited microorganisms  
 7. ☐ nucleotide and/or amino acid sequence listing (diskette)  
 8. ☐ other (specify):

Figure No. \_\_\_\_\_ of the drawings (if any) should accompany the abstract when it is published.

**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

BOEHRINGER INGELHEIM INTERNATIONAL GMBH  
ppa. i.A.


Dr. D. Laudien



DI Christine Farniok

For receiving Office use only

1. Date of actual receipt of the purported international application:	(11.11.97) 11 NOV 1997	2. Drawings: <input checked="" type="checkbox"/> received: <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority specified by the applicant: ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid	

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